

II. REMARKS

Formal Matters

Claims 1, 3, 4, and 21-27 are pending after entry of the amendments set forth herein.

Claims 1, 3, 4, and 21-27 were examined and were rejected. Claims 5-20 were withdrawn from consideration.

Claims 1, 21, and 24-27 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. No new matter is added by these amendments.

Claims 5-20 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Objection to the specification

The specification was objected to. The Office Action stated that the amendments made to paragraph 0049 in the response filed on March 2, 2007 add new matter.

As set forth in MPEP §2163.07(II), an amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction.

The amendments to paragraph 0049 were made to correct obvious typographical errors, and as such do not add new matter.

In the response, filed on March 2, 2007, paragraph 0049 was amended as follows:

For example, an apoE stable folding intermediate is produced in significant amounts in conditions of about 2 M to about 7M urea. As detected by far-ultraviolet (uv) circular dichroism (CD) an apoE4 stable folding intermediate is maximally abundant (i.e. approximately 90% of total apoE) in a solution of apoE at pH 4.0 in about 3.5 M to about 4.5 M urea. An apoE4 stable folding intermediate is approximately 50% abundant in about 3.0 M urea to about 6.0 M

urea. Virtually no apoE4 ~~an apoE4 stable folding intermediate~~ can be detected below 2.0 M urea, at least by far-uv CD. As detected by far-uv CD, an apoE3 ~~an apoE4~~ stable folding intermediate is maximally abundant (i.e. approximately 80% of total apoE) in a solution of apoE at pH 4.0 in about 4.5 M to about 5 M urea. An apoE3 ~~an apoE4~~ stable folding intermediate is approximately 50% abundant in about 3.8 M urea to about 6.0 M urea. Virtually no apoE3 molten globule can be detected below 2.5 M urea, at least by far-uv CD.

Paragraph 0049 as originally filed included obvious typographical errors, as shown above.

Those skilled in the art would recognize the existence of the errors in paragraph 0049, and would also recognize the appropriate correction.

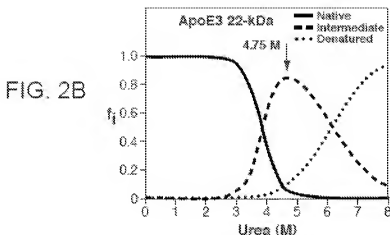
Paragraph 0049 as amended states that an apoE3 stable folding intermediate is maximally abundant (i.e., approximately 80% of total apoE) in a solution of apoE at pH 4.0 in about 4.5 M to about 5 M urea. This range is supported in paragraph 00169.

Paragraph 00169 reads as follows:

Figures 2A and 2B show the fraction of folded, intermediate and unfolded protein for apoE3 and apoE4 according to the three-state model. The concentration of urea at which the folding intermediate was at maximum concentration was 3.75 M for the apoE4 22-kDa fragment ($\approx 90\%$) and 4.75 M for the apoE3 fragment ($\approx 80\%$). These results demonstrate that in urea the folding intermediate is a stable thermodynamic state—the first criterion for a molten globule.

Paragraph 00169 indicates that the concentration of urea at which the folding intermediate was a maximum concentration was 4.75 M for apoE3. The concentration 4.75 M is within the “about 4.5 M to about 5 M” range recited in claim 27. Thus, paragraph 00169 provides support for the amendment in paragraph 0049 to read, “As detected by far-uv CD, an apoE3 ~~an apoE4~~ stable folding intermediate is maximally abundant (i.e. approximately 80% of total apoE) in a solution of apoE at pH 4.0 in about 4.5 M to about 5 M urea.”

Paragraph 00169 discusses the data shown in Figures 2A and 2B, and states that the concentration of urea at which the folding intermediate was at maximum concentration was 4.75 M for the apoE3 fragment ($\approx 80\%$).



As shown in Figure 2B, an apoE3 stable folding intermediate is approximately 50% abundant in about 3.8 M urea to about 6.0 M urea, and is approximately 80% abundant in about 4.5 M urea to about 5 M urea, as described in paragraph 0049 as amended.

The amendments to paragraph 0049 were made to correct obvious typographical errors. Given the discussion in paragraph 00169, and the data shown in Figure 2B, those skilled in the art would recognize the existence of the errors in paragraph 0049, and would also recognize the appropriate correction. As such, no new matter is added by the amendments to paragraph 0049.

Rejection under 35 U.S.C. §112, first paragraph

Claims 26 and 27 were rejected under 35 U.S.C. §112, first paragraph, as allegedly reciting new matter.

The Office Action stated that newly presented claims 26 and 27 are considered new matter on the basis of the “new matter” objection to the specification. Applicants respectfully traverse the rejection.

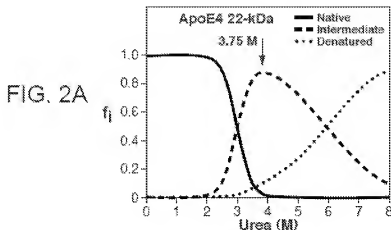
Claim 26

Claim 26 depends from claim 1 and recites that the apoE stable folding intermediate is formed at a urea concentration of from about 3.5 M to about 4.5 M.

Paragraph 0049 states:

As detected by far-ultraviolet (uv) circular dichroism (CD) an apoE4 stable folding intermediate is maximally abundant (i.e. approximately 90% of total apoE) in a solution of apoE at pH 4.0 in about 3.5 M to about 4.5 M urea.

The above-quoted sentence of paragraph 0049 is the text as originally filed. The fact that an apoE4 stable folding intermediate is maximally abundant in about 3.5 M urea to about 4.5 M urea is also shown in Figure 2A, which is reproduced below.



As such, claim 26 does not recite new matter.

Nevertheless, and solely in the interest of expediting prosecution, claim 26 is amended to recite “wherein the apoE is apoE4, and wherein the apoE stable folding intermediate is formed at a urea concentration of from [[about]] 3.5 M to [[about]] 4.5 M.”

Claim 27

Claim 27 depends from claim 1 and recites that the apoE stable folding intermediate is formed at a urea concentration of from about 4.5 M to about 5 M.

As discussed above, paragraph 0049, paragraph 00169, and Figure 2B provide support for the recitation of a urea concentration of from about 4.5 M to about 5 M. As such, no new matter is added by claim 27.

Nevertheless, and solely in the interest of expediting prosecution, claim 27 is amended to recite “wherein the apoE is apoE3, and wherein the apoE stable folding intermediate is formed at a urea concentration of from [[about]] 4.5 M to [[about]] 5 M.”

Conclusion as to the rejection under 35 U.S.C. §112, first paragraph

Applicants submit that the rejection of claims 26 and 27 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C. §112, second paragraph

Claims 1, 3, 4, and 21-27 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

The Office Action objected to the word “about” and the phrase “at least about.”

Without conceding as to the correctness of this rejection, and solely in the interest of expediting prosecution, claims 1, 21, and 24-27 are amended to delete the word “about.”

Conclusion as to the rejection under 35 U.S.C. §112, second paragraph

Applicants submit that the rejection of claims 1, 3, 4, and 21-27 under 35 U.S.C. §112, second paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL-282.

Respectfully submitted,
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Date: June 9, 2008

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